UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND
TOXIC SUBSTANCES

June 15, 1999

MEMORANDUM

EPA Reg. No.: 67505-5 ECTO F724 PRODUCT
DP Barcode: D253533
Case No: 060802
PC Code: 129032 Pyriproxyfen, Nylar

From: Byron T. Backus, Ph.D., Toxicologist
Technical Review Branch
Registration Division (7505C)

Byron T. Backus 6/15/99

To: Joseph Tavano/Arnold Layne PM 03
Insecticide Branch
Registration Division (7505C)

Registrant: ECTO DEVELOPMENT CORP.

ACTION REQUESTED: "Review data and label for Companion Animal Safety for ferrets. MRID 447561-01."

BACKGROUND: According to a cover letter from the registrant, this is an amendment to an existing registration to use this product on ferrets. The package includes a Companion Animal Safety Study (MRID 44756102) on ferrets. This study was conducted at Stillmeadow Inc. (12852 Park One Drive, Sugar Land, TX 77478). This study was reviewed at Oak Ridge, and the resulting DER was secondarily reviewed and modified by TRB staff, before being sent to HED.

COMMENTS AND RECOMMENDATIONS:

The following is the executive summary from the DER for MRID 44756102:

In a companion animal safety study (MRID 44756102) ECTO F724 (Active Ingredient: Pyriproxyfen: 5.3%) was topically applied two times (with 21 days between applications), at 1X, 3X and 5X dose levels (1.5, 4.5 and 7.5 mL/ferret, respectively), to groups of six male and six female 16-19 week-old ferrets. Controls were treated with 7.5 mL tap water. The test animals were observed for pharmacologic and/or toxicologic effects within the first 10 min after treatment, at 1, 2, 4 and 6 hr after treatment, and daily thereafter until the end of the study on Day 36. Body weights were recorded on Days -14, -7, -1 and weekly (Days 7, 14, 21, 28, and 36) during the study. Food consumption was monitored daily. Blood samples were obtained from the jugular vein approximately one week prior to testing and on the day following the initial dosing; blood was also sampled from selected animals on the day following the second dosing. The ferrets were anesthetized before blood was taken. Due to the difficulty of bleeding ferrets, blood could not be obtained from all animals, and in some cases a sufficient amount was obtained only for serum chemistry (not hematology).

No mortality occurred and no toxicologic or pharmacologic effects or erythema, edema, or other skin effects were observed at any time during the study. One animal in the 5X group was found to have a teratoma in the mid-abdominal area; this animal was replaced with another which was dosed on Day 2. One 5X male was very thin on Days 14 through Day 17, but this was not considered to be related to the treatment. One control animal was very thin on Day 8 through Day 15. Food consumption in males was consistent among groups; food consumption in females varied among groups; however, the differences were not dose-dependent. There were no treatment-related, biologically-significant effects on clinical biochemistry, or hematology. Sporadic fluctuations in potassium, BUN, ALT and AST in some test animals were not considered to be caused by the test substance.

This study followed the pertinent guidelines for a companion animal safety study (OPPTS 870.7200) and also is generally consistent with the product labeling and application instructions which state that it should not be used more often than once every three weeks. However, the proposed labeling specifies that it is not to be used on animals younger than 12 weeks of age, while the animals in this study were 16-19 weeks old. Labeling should be revised to state that the product is not to be used on ferrets younger than 16 weeks of age. Otherwise, the required 5X margin of safety has been demonstrated and the study is **Acceptable.**